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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER |
|---|
| O HARA, EILEEN B |

| ART UNIT | PAPER NUMBER |
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| 1646 | 9 |

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 10/041,574 | Applicant(s) NI ET AL. | |
|---|---|---|---|
| | Examiner Eileen O'Hara | Art Unit 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,14,20 and 25-126* is/are pending in the application.

4a) Of the above claim(s) *1,14 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-126* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,14,20 and 25-126* ~~are~~ were subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

1. Claims 1, 14, 20 and 25-126 are pending in the instant application. Claims 2-13, 15-19 and 21-24 have been canceled and claims 25-126 have been added as requested by Applicant in Paper Number 7, filed May 7, 2003.

### *Election/Restriction*

2. Applicant's election with traverse of Group VIII in Paper No. 7 is acknowledged. The traversal on pages 15-17 of the response is on the ground(s) that MPEP §-803 lists the criteria for a proper restriction as an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent or distinct, and if the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions. Applicants assert that even assuming that the groups listed by the Examiner represented distinct or independent inventions, restriction remains improper unless it can be shown that the search and examination of the groups would entail a "serious burden", and that no such showing has been made. Also argued is that a search of the claims of group I would also provide useful information for the claims of groups II through VIII, while a search of the claims of group VII would also provide useful information for the claims of groups I through VI and VIII, and that in many if not most publications disclosing a polynucleotide, the authors also routinely include polypeptides encoded thereby as well as antibodies that bind such polypeptides. Applicants also argue that since the searches for polynucleotides, polypeptides and antibodies commonly overlap, the search and examination of a

polynucleotide and the corresponding polypeptides as well as antibodies it binds, would not entail a serious burden.

This is not found persuasive because consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search:. These criteria were met for groups I-VIII in the above restriction. A search for antibodies to a protein would constitute a different search than that of a search for the protein. It is old and well known in the art that antibodies have been generated without having purified protein, and antibodies to one protein may also cross-react with a related protein. Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious.

Applicants also assert that as Groups I-VI are in the same class and subclass, so that contrary to the Examiner's assertion, they have not "acquired a separate status in the art because of their different classification", and would not present a serious burden to search and examine together.

Applicants' arguments have been fully considered but are not deemed persuasive. Contrary to Applicants' assertion, on page 4 of Paper No. 6 it was stated that "these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their different classification, recognized divergent subject matter, **and/or** the need for non-coextensive literature **and/or** separate sequence database searches". The nucleic acid sequences of groups I-VI are different and would therefore require separate sequence searches, which would be a serious burden. As stated in the MPEP § 803, "a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate

classification, separate status in the art, or a different field of search as defined in MPEP § 808.02.".

It is additionally pointed out that the search and examination of each of the groups, which searches and examinations are not-co-extensive, are not required one for the other. Thus, contrary to applicant's position, the search and examination of each group would indeed pose a serious burden for the examination. Also argued is that a search for one group would be overlapping and provide useful information about the other groups. However, the fact that some useful information may be obtained in the searches of one group for that of another group, and the fact that there may possibly be overlaps in the searches is not a sufficient basis for holding the restriction to be improper, because the search and examination of one group may not yield all of the necessary information for the other group. Thus, the groups require divergent searches, and to search all inventions would be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 14 and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claims 25-126 are currently under examination.

***Priority***

3. This application filed under former 37 CFR 1.60 lacks the current status of the nonprovisional parent application 09/527,236. A statement reading "(now United States Patent No. 6,358,508)" should be included after "09/527,236, filed March 16, 2000" following the title on the first sentence of the specification.

***Specification***

4.1 The abstract of the disclosure is objected to because it does not recite the invention to which the claims are directed, antibodies. Correction is required. See MPEP § 608.01(b).

4.2 The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Antibodies to Human Tumor Necrosis Factor Receptor TR9.

***Information Disclosure Statement***

5. In the IDS filed May 7, 2003, (Paper No. 8), Applicants state that the portions of U.S. Patent Applications 09/912,293 and 09/912,292, were submitted with the IDS. However, these documents were not present in the file. If Applicants wish these to be considered, it is suggested that these documents be submitted along with the response to this office action.

The sequences disclosed in the IDSs filed May 7, 2003 and January 10, 2002 (references AS-BE and BH-BN of IDS No. 3 and references AK-AW, BA and BB of IDS No.8) have been considered to the extent that was possible absent an explanation of relevance or a sequence alignment.

***Advisory Information***

6. The claims are interpreted such that the fragment of the antibody must also bind the protein. If Applicants intend otherwise, it is suggested the claims be amended to clarify this.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 25-28, 30-53, 55-76, 78-101 and 103-126 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,358,508. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of U.S. Patent No. 6,358,508 are drawn to an isolated antibody or fragment thereof which binds to a protein whose sequence consists of amino acids 283-308 of SEQ ID NO: 2, and compositions thereof, while claims 25-28, 30-53, 55-76, 78-101 and 103-126 of the instant invention are drawn to an isolated antibody or fragment thereof which binds to a protein consisting of amino acids –40 to 615, 1-615, 1-310, or 30 or 50 contiguous amino acids of SEQ ID NO: 2. The species of antibody to amino acids 283-308 of SEQ ID NO: 2 anticipate the genus claims of the instant application, drawn to antibody to the larger portions of the protein. Claims 29, 54, 77 and 102 are not included because they are drawn to antibody to protein consisting of amino acids 27-171 of SEQ ID NO: 2, and an antibody to amino acids 283-308 would not bind to a protein consisting of amino acids 27-171. It would be *prima facie* obvious to one of ordinary skill in the art to make the antibody in different forms such as human,

chimeric, humanized, single chain, as encompassed by the claims, since these modified forms of antibodies are well known in the prior art. It would also be *prima facie* obvious to one of ordinary skill in the art to make a fusion protein comprising the antibody and a heterologous polypeptide, for example to target a heterologous polypeptide to a cell that would express the protein of SEQ ID NO: 2, or to attach the antibody to a solid support, in order to easily purify the protein of SEQ ID NO: 2. It would also be *prima facie* obvious to one of ordinary skill in the art to make a hybridoma cell that would produce monoclonal antibodies to the protein of SEQ ID NO: 2.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 73-120 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims require the specifically disclosed cDNA. Applicants' referral to the deposit of the cDNA clone deposited as ATCC Deposit Number 209037 on page 9 of the specification is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. If the deposits were made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and

registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State. Additionally, amendment of the specification to recite the date of the deposit, the complete name and address of the depository, and the accession number of the deposited cell line is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 25-126 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25-126 are indefinite because they encompass an antibody or fragment thereof that "specifically" binds to a polypeptide. The specification does not define the term "specifically binds" and since it is a relative term, it is not clear what this means. The rejection would be withdrawn if the word "specifically" were deleted.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 25-33, 35-37, 41, 44-58, 60, 61, 65, 68-81, 83-85, 89, 92-106, 108, 109, 113, 116-122 and 124-126 are rejected under 35 U.S.C. 102(e) as being anticipated by Deen et al., U.S. Patent No. 6,013,476 (cited by Applicants).

Claims 25-33, 35-37, 41, 44-58, 60, 61, 65, 68-81, 83-85, 89, 92-106, 108, 109, 113, 116-122 and 124-126 encompass antibody or fragment thereof that binds to the protein of SEQ ID NO: 2 (encoded by the cDNA contained in ATCC Deposit Number 20937), or the specific portions of the protein recited in the claims, or at least 30 or 50 contiguous amino acids of SEQ ID NO: 2, wherein the protein may be glycosylated, and wherein the antibody or fragment thereof may be polyclonal, monoclonal, chimeric, single chain, humanized or an Fab fragment, may be labeled and which may agonize signaling, and which may bind protein in a Western blot or ELISA, cell producing antibody and method of detecting protein in a biological sample.

Deen et al. disclose a protein (SEQ ID NO: 2) that is 100% identical to the protein of SEQ ID NO: 2 of the instant invention (see attached alignments), and antibodies to the protein. It should be noted that there is a mismatch at amino acid 24, which in patent 6,013,476 is arginine and in the instant application is threonine; however, the nucleic acid sequence of patent

6,013,476 (SEQ ID NO: 1, open reading frame from nucleotides 7-1971) shows that the nucleic acid sequence that encodes amino acid 24 (nucleotides 76-78 of SEQ ID NO: 1) is ACG, which actually encodes threonine. The protein sequence was deduced from the nucleic acid sequence, and it is the nucleic acid sequence that is controlling. Therefore, the proteins of the instant application and patent 6,013,476 are identical.

Deen et al. (Patent 6,013,476) has a filing date of 10/28/97, and claims priority to provisional 60/041,769, which has a filing date of 4/2/97. The effective filing date of the instant application is 6/11/97 (provisional 60/052,991). Therefore, Deen et al. has an earlier priority date. However, provisional 60/041,769 of Deen et al. did not disclose the entire polypeptide sequence of SEQ ID NO: 2. Provisional 60/041,769 disclosed a polypeptide sequence that is identical to amino acids –14 to 48 and 51-84 of SEQ ID NO: 2 of the instant application (see attached sequence alignment). Therefore, Deen et al. provisional 60/041,769 does not disclose the majority of the 655 amino acid full-length protein of SEQ ID NO: 2 of the instant application. However, the claims as written encompass antibodies that would bind to the polypeptide disclosed in provisional 60/041,769, since they encompass antibodies that would bind to a polypeptide comprising amino acids –14 to 84 of SEQ ID NO: 2 or at least 30 or 50 contiguous amino acids of SEQ ID NO: 2, and are therefore anticipated by Deen et al. Deen et al. also teaches that the protein may be glycosylated (column 3, line 37 to column 4, line 1), and wherein the antibody or fragment thereof may be polyclonal, monoclonal, chimeric, single chain, humanized or an Fab fragment (column 3, lines 1-5, column 16, lines 1-26), may be labeled (column 17, lines 55-60) and which may agonize signaling (column 17, lines 16-20), and which may bind protein in a Western blot or ELISA (column 15, lines 7-26 and column 18, lines 6-16),

cell producing antibody (column 16, lines 9-21) and method of detecting protein in a biological sample (column 15, lines 7-26). Therefore, Deen et al. anticipates the claims.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11.1 Claims 40, 64, 88 and 112 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deen et al., U.S. Patent No. 6,013,476, and further in view of Abrams et al., U.S. Patent No. 5,112,954, May 12, 1992.

Claims 40, 64, 88 and 112 encompass antibody or fragment thereof that binds to the protein of SEQ ID NO: 2 (encoded by the cDNA contained in ATCC Deposit Number 20937), or the specific portions of the protein recited in the claims, or at least 30 or 50 contiguous amino

acids of SEQ ID NO: 2, wherein the antibody or fragment thereof is conjugated to a cytotoxic agent.

The teachings of Deen et al. are described above. Deen et al. do not teach that the antibody or fragment thereof is conjugated to a cytotoxic agent.

Abrams et al. teach that cytotoxic agents can be conjugated to antibodies to target specific cells, enhancing the cytotoxic effect on target cells compared to non-target cells (see entire patent, and especially abstract, and column 5, line 65 to column 6, line 11).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use Deen et al.'s antibodies and conjugate them with a cytotoxic agent, as taught by Abrams et al., in view of Abrams et al.'s suggestion that it would be desirable to do so, as cited above. The skilled artisan would be motivated to do so in order to target cytotoxic agents to particular cell types that express the receptor of SEQ ID NO: 2 on the cell surface, and there would be a reasonable expectation of success, since the method of conjugating compounds to antibodies that has been widely and successfully used in the field of molecular biology.

11.2 Claims 42, 43, 66, 67, 90, 91, 114 and 115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deen et al., U.S. Patent No. 6,013,476, and further in view of Chester et al., U.S. Patent No. 5,876,691, March 2, 1999.

Claims 42, 43, 66, 67, 90, 91, 114 and 115 encompass antibody or fragment thereof that binds to the protein of SEQ ID NO: 2 (encoded by the cDNA contained in ATCC Deposit Number 20937), or the specific portions of the protein recited in the claims, or at least 30 or 50

contiguous amino acids of SEQ ID NO: 2, wherein the antibody or fragment thereof is fused to a heterologous polypeptide or attached to a solid support.

The teachings of Deen et al. are described above. Deen et al. do not teach that the antibody or fragment thereof is fused to a heterologous polypeptide or attached to a solid support.

Chester et al. teach that a His tag (heterologous polypeptide) can be fused to an antibody, and that the fusion antibody can then be purified by binding it (attaching it) to a solid support containing metal ions that bind the His tag (see column 6, lines 5-52 and column 15, lines 20-49).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use Deen et al.'s antibody and fuse it to a heterologous polypeptide such as a His tag and then purify the antibody by binding it to a solid support, as taught by Chester et al., in view of Chester et al.'s suggestion that it would be desirable to do so, as cited above. The skilled artisan would be motivated to do so, because Chester et al. teaches that a higher yield may be achieved, the scale-up is relatively simple and less costly than previous methods of purification, and the risk of antigen leaching from the column is eliminated, so that this method more easily and efficiently purifies the antibodies to a level suitable for clinical use. There would be a reasonable expectation of success, since the method of making fusion proteins was well known and successfully used in the field of molecular biology, and Chester et al. demonstrates that the antibody purification technique worked well.

11.3 Claims 34, 38, 39, 59, 62, 63, 82, 86, 87, 107, 110, 111 and 123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deen et al., U.S. Patent No. 6,013,476, and further in view of Jakobovits et al. et al., U.S. Patent No.6,235,883, May 22, 2001.

Claims 34, 38, 39, 59, 62, 63, 82, 86, 87, 107, 110, 111 and 123 encompass antibody or fragment thereof that binds to the protein of SEQ ID NO: 2 (encoded by the cDNA contained in ATCC Deposit Number 20937), or the specific portions of the protein recited in the claims, or at least 30 or 50 contiguous amino acids of SEQ ID NO: 2, wherein the antibody or fragment thereof is a human antibody, and can be radiolabeled or biotinylated. The teachings of Deen et al. are described above. Deen et al. do not teach that the antibody or fragment thereof is a human antibody or can be radiolabeled or biotinylated.

Jakobovits et al. teach that fully human antibodies can be made, and could be labeled with either a radiolabeled amino acid or biotynoyl moieties (see entire patent, and especially the abstract and column 2, line 13 to column 4, line 42, column 18, lines 25-46, column 22, lines 15-25, and column 35, lines 29-49). Jakobovits et al. state in these sections:

"Furthermore, such a strategy could provide an ideal source for production of fully human monoclonal antibodies (Mabs)--an important milestone towards fulfilling the promise of antibody therapy in human disease. Fully human antibodies are expected to minimize the immunogenic and allergic responses intrinsic to mouse or mouse-derivatized Mabs and thus to increase the efficacy and safety of the administered antibodies. The use of fully human antibodies can be expected to provide a substantial advantage in the treatment of chronic and recurring human diseases, such as inflammation, autoimmunity, and cancer, which require repeated antibody administrations."

"As used herein, the terms "label" or "labeled" refers to incorporation of a detectable marker, e.g., by incorporation of a radiolabeled amino acid or attachment to a polypeptide of biotinyl moieties that can be detected by marked avidin (e.g., streptavidin containing a fluorescent marker or enzymatic activity that can be detected by optical or colorimetric methods). "

"The detection antibodies used in ELISA experiments were goat anti-mouse IgG-HRP (Caltag, M-30107), goat anti-mouse Ig.kappa.-HRP (Caltag, M 33007), mouse anti-human IgG2-HRP

(Southern Biotechnology, 9070-05), mouse anti-human IgM-HRP (Southern Biotechnology, 9020-05), and goat anti-human kappa-biotin (Vector, BA-3060)."

"Imaging Agent: Through binding a radionuclide (e.g., yttrium (.sup.90 Y)) to antibodies in accordance with the present invention, it is expected that radiolabeled antibodies in accordance with the present invention can be utilized as a diagnostic, imaging agent."

Jakobovits et al. teach the advantages of providing human antibodies for therapeutic purposes, and that antibodies can be labeled with biotin for use in assays such as ELISAs and that radiolabeled antibodies can be used for diagnostic imaging.

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use Deen et al.'s antibody and make them fully human, to radiolabel them or biotinylate them, as taught by Jakobovits et al. in view of Jakobovits et al.'s suggestion that it would be desirable to do so, as cited above. The skilled artisan would be motivated to do so, because Jakobovits et al. teach teach the advantages of providing human antibodies for therapeutic purposes, and that antibodies can be labeled with biotin for use in assays such as ELISAs and that radiolabeled antibodies can be used for diagnostic imaging. There would be a reasonable expectation of success, since the method of labeling such antibodies was well known and successfully used in the field of molecular biology, and Jakobovits et al. demonstrates that the human antibody worked well in experiments.

***Conclusion***

12.1 No claim is allowed.

12.2 Antibodies that bind to a polypeptide consisting of amino acids 85 to 615 of SEQ ID NO: 2 are free of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306. Official papers After Final filed by RightFax should be directed to (703) 872-9307. Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Eileen B. O'Hara

Patent Examiner